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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/844,516   | 04/27/2001  | Julie E.M. McGeoch   | H0498/7095 TJO      | 9062             |
| 7590   | 06/15/2004  |                      | EXAMINER            |                  |
| Timothy J. Oyer<br>Wolf, Greenfield & Sacks, P.C.<br>600 Atlantic Avenue<br>Boston, MA 02210 |             |                      | OLSEN, KAJ K        |                  |
|  |             |                      | ART UNIT            | PAPER NUMBER     |
|  |             |                      | 1753                |                  |

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                 |                |
|------------------------------|-----------------|----------------|
| <b>Office Action Summary</b> | Application No. | Applicant(s)   |
|                              | 09/844,516      | MCGEOCH ET AL. |
| Examiner                     | Art Unit        |                |
| Kaj K Olsen                  | 1753            |                |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM  
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 22 March 2004.  
 2a) This action is FINAL.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-54 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-54 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 27-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 27 is drawn to a method, but the claim doesn't specify what the method is.

Applicant should explicitly state in the preamble of the claim what the method is drawn to (see claim 36 for a definitive preamble). Applicant traverses the rejection, but merely responds with general case law. This is not persuasive. The claim is currently drawn to a method, but doesn't explain what the method even is for in the preamble. Moreover, the examiner is confused by this traversal. This claim would be considered definite if the applicant merely added some simple preamble (e.g. --A method for measuring ion-channel oscillations--). This would not narrow the scope of the claim because it is merely incorporating subject matter from the body of the claim. What is objectionable about simply requesting a claim have a preamble that defines what the invention is?

4. The examiner has withdrawn the previous rejections of claims 28 and 33, but will continue to give those terms their broadest reasonable interpretation.

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-13, 15-21, 24-26, 34, 35, and 46-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Ikematsu et al (USP 5,503,744) with evidence provided by the UCSD Transport Protein Database.

7. These claims were previously rejected over the teaching of Ikematsu (see previous office action for details). Applicant has amended the various independent claims in various manners where reference to binding of the analyte to pores or ion channels to result in a second frequency of oscillation. However, it doesn't appear any of these amendments reads free of the teaching of Ikematsu. With respect to amended independent claims 1, 25 and 48-50, applicant has only stated that the pore or ion-channel is (using claim 1 as an example) "able to bind an analyte". This is not setting forth any actual structure that reads free of Ikematsu. Presumably there are a number of chemicals that would be capable of binding to the ion-channel of Ikematsu and any binding to the ion-channel would change the dynamics of how it oscillates. Similarly, independent claims 34 and 46 only state (using claim 34 as an example) "wherein binding of the analyte to the oscillating ion channel alters the frequency". Again, this doesn't appear to be further limiting the actual device itself.

8. The examiner has withdrawn the rejection of claims 27-33 over Ikematsu because Ikematsu does not actually teach the steps of allowing the oscillating channel bind to the analyte and the measuring of a second frequency.

9. Claims 25, 27-33, 36, 38-43, 45, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McGeoch et al (Brain Research 766 (1997), pp. 188-194).

10. These claims were previously rejected over the teaching of McGeoch (see previous office actions for details). Applicant has amended independent device claims 25 and 46 in the manner the examiner addressed above with respect to Ikematsu. As discussed there, the amended claims do not actually specify any additional structure and remain rejected over the teaching of McGeoch. In addition, McGeoch is drawn to the same ATP synthase subunit c of the present invention, which clearly evidences that the ion-channel of McGeoch would inherently be capable of binding to an analyte and altering the frequency. With respect to independent method claims 27 and 36, McGeoch already showed that the analyte will cause the frequency of oscillations to vary (see fig. 2). Applicant urges that McGeoch does not disclose that the current oscillations are altered upon binding of subunit to the analyte. The examiner disagrees. In particular, McGeoch discusses the various conditions necessary for forming the oscillations including controlling the choline and calcium concentrations to get the desired oscillations (p. 192, second column). This described varying of the analytical conditions to get the desired response would read on the specified first and second frequencies. In fact, claim 36 doesn't even require a first frequency be measured. It just states that a first frequency is an inherent property that is varied by the addition of analyte. Neither claims 27 nor 36 require the frequencies to be utilized for the

detection. Claim 27 has no preamble (which is still indefinite). Although claim 36 mentions detecting a sample, there is nothing in the body of the claim requiring the frequency measurement be utilized for anything. Although McGeoch does not appear to explicitly disclose the frequency was changing as a result of analyte binding to the ion-channel, that appears to be evidenced by the instant invention (again, McGeoch is drawn to same disclosed ATP synthase subunit c of the present invention). Hence the binding limitations of claims 27 and 36 are an inherent part of the method of McGeoch. Although the present inventors may have discovered that the analyte is binding with the ion-channels, a patent cannot be granted for discovering something that was already an inherent function in the prior art.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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13. Claims 1, 2, 6-24, 26, 34, 35, 47, 49-51, 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGeoch in further view of Alberts et al (Molecular Biology of the Cell, Third Edition, 1994).

14. McGeoch set forth all the limitations of these claims but did not explicitly set forth the electrolyte reservoirs and insulating barriers of these claims. McGeoch appears to rely on conventional patch clamping techniques for measuring the oscillating currents (see section 2.4 on p. 189). Alberts teaches how conventional patch clamps can be performed. Namely, a pipette (i.e. an insulating layer) with a hole present has a cell membrane that forms across the surface of the hole where the membrane contains the ion-channel (i.e. the pore) (see fig. 4-55 and discussion accompanying it). The inside of the pipette would constitute one electrolyte container while the solutions on the other side of the pipette would be a separate electrolyte, and whatever container contains that electrolyte (e.g. beakers, etc) would constitute another electrolyte reservoir. McGeoch teaches in section 2.4 what fluids should be present in each of these reservoirs. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Alberts for the patch clamp experiments of McGeoch because the use of conventional structure for the performance of specific experiments requires only routine skill in the art.

15. With respect to the use of an array of holes, it would have been obvious to one having ordinary skill in the art at the time the invention was made to utilize an array of holes since it has been held that mere duplication of the essential working parts of a device involves only routine skill in the art. St. Regis Paper Co. v. Bemis Co., 193 USPQ 8.

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16. Claims 14, 32 and 53-55 (and claims 1-13, 15-21, 24-26, 34, 35, and 46-52 in the alternative) are rejected under 35 U.S.C. 103(a) as being unpatentable over Ikematsu in view of McGeoch.

17. Ikematsu set forth all the limitations of these claims, but did not disclose the particular use of the subunit c of ATP synthase as the oscillating protein. As discussed above, McGeoch disclosed this particular protein and disclosed that this protein provides the desired oscillations with a large range of oscillating frequencies (see “4. Discussion” starting on p. 193). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of McGeoch for the oscillating protein of Ikematsu because this protein has been identified as a viable candidate providing a large range of oscillating frequencies.

18. In response, applicant urges that the examiner has not pointed to disclosure in Ikematsu about the desirability of a large range of frequencies. First, why does the applicant believe it is necessary for the primary teaching to provide the motivation? The suggestion or motivation to combine teachings need not come from the primary teaching, but can come any of the references or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Second, applicant is ignoring the fact that Ikematsu draws those with ordinary skill in the art to the use of other known oscillating membranes col. 7, lines 30-36. Because McGeoch discloses other desirable oscillating ion-channels known in the art (and provided motivation for utilizing those membranes), one possessing ordinary skill in the art would have been motivated to look to these desirable oscillating ion-channels for those reasons.

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19. With respect to the claims in the alternative, if applicant urges that the particular ion-channel of Ikematsu would not be capable of binding with any unspecified analyte (although applicant has only argued that Ikematsu doesn't teach any binding and is silent on whether Ikematsu could bind with an analyte), the present invention evidences that subunit c of ATP synthase does have that specified property and would clearly read on the new limitations of 1, 25, 34, 46, and 48-50.

20. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over McGeoch in view of WO 97/05477 (hereafter "WO '477").

21. McGeoch set forth all the limitations of the claim, but did not specify derivatizing the ion channel with functional groups to detect a predetermined analyte. WO '477 teaches in an alternate sensor relying on ion channels that functional groups can be added to ion channels so that different analytes can be sensed with a given ion channel (p. 9, line 33 through p. 10, line 31). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of WO '477 for the method of McGeoch in order to increase the utility of the oscillating device to other analytes.

### *Conclusion*

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kaj Olsen whose telephone number is (571) 272-1344. The examiner can normally be reached on Monday through Thursday from 6:30 A.M. to 4:00 P.M. and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kaj Olsen Ph.D.  
Primary Examiner  
AU 1753  
June 10, 2004